REMARKS

Claims

Claims 1, 51-57, 64, 65, and 67 and 68 are currently under examination. Claims 2–50, 58–61 and 66 are cancelled without prejudice or disclaimer and claims 58-63 and 69-104 withdrawn from consideration due to restriction/election.

Claim 105 is added by this paper.

Claim amendments

Applicants' amendment of claim 1 is not to be construed with acquiesce to any ground of rejection. Support for the polypeptide structures recited in the claims can be found in, for example, the paragraph bridging pages 9 and 10, and the disclosure contained in the paragraphs bridging page 11, line 12 to page 12, line 23 of the originally-filed specification. Support for the hybridization language can be found in, for example, page 13, ¶1; page 13, lines 11–20 and the disclosure contained in Example 10, of the originally-filed specification. Support for the functional aspect recited in the claim can be found in, for example, page 1, ¶1 and the paragraph bridging pages 3 and 4 of the originally-filed specification.

Amended claim 21 is directed to the polypeptide of the instant invention. The amendment of claim 71 is self-explanatory.

It is respectfully submitted that the claim amendments do not raise new matter.

New claim 105, which depends on Applicants' instant claim 1, recites polypeptides that are 95% identical to the elected polypeptide of SEQ ID NO: 2. Inasmuch as the instant claim 1 recites a broader claim term (i.e., 90% identity), it is respectfully submitted that a search and examination of the new dependent claim does not impose additional search burden on the PTO. Entry thereof is earnestly solicited.

Restriction/Objection

It is respectfully submitted that the objection of claim 1 is moot in view of the amendments. However, the following comments are made with respect to the PTO's contention that the scope of the claims "must be restricted to elected subject matter only." Applicants reserve the right to reintroduce cancelled subject matter during prosecution.

In Reply to the Restriction Requirement dated October 17, 2006, Applicants

timely elected, with traverse, Group I (claims 1, 51–57, and 64–67) drawn to an isolated polypeptide and/or compositions thereof.

The election of the polypeptide comprising of SEQ ID NO: 2 and fragments thereof was made with traverse in accordance with the provisions set forth in the MPEP.

In the present Office Action and in the restriction requirement of record, the Examiner is requiring Applicants to elect claims directed to a single species, for example, the polypeptide of SEQ ID NO: 2. This is improper insofar as the restriction requirement carves a generic invention, for example, product claims directed to a polypeptide and/or compositions thereof, into several Groups of inventions (Groups I, II and III). The polypeptides of SEQ ID NOs: 2, 4, and 6 are generic to the claimed invention. Under such scenario, the MPEP expressly states that a proper manner of restriction would be to make an election of species requirement. In compliance with such provisions, Applicants timely elected the polypeptide species of SEQ ID NO: 2 in the reply filed November 17, 2007.

The Examiner is encouraged to examine the broadest possible scope of invention indicated by the elected species. It is improper for the PTO to refuse to examine in one application the entire scope of the claims therein unless they lack unity of invention. The Office Action has not fully demonstrated how expansion of the search to include other related species (for example, the polypeptide of SEQ ID NOs: 4 or 6) would be burdensome. Therefore, a modification of the pending restriction requirement to at least include the claims allegedly drawn to non-elected species is respectfully requested.

The PTO is cordially requested to withdraw the restriction requirement in its entirety inasmuch as it is submitted that the claims comply with the PCT Rules for unity of invention. Annex B under PCT Rule 13.1 states that, in a Markush claim such as the present one, the technical relationship or corresponding special technical feature *is considered to be met* when all alternatives have a common property or activity and a common structure is present. Such a common structure is clearly present in the polypeptides of the instant invention. Moreover, common properties are present inasmuch as the claimed oxidase activity is generic to the polypeptides of the instant invention. Thus, the unity of invention requirement is clearly met. The Examiner is respectfully requested to examine the full scope of the claims on their merits.

Withdrawal of the objection is respectfully requested.

Rejoinder

The claims in Group 10 (claims 71, 75, and 79), which are drawn to a method of diagnosing or treating diseases, and the claims in Group 19 (claims 83–92), which are drawn to a method for modulating the level and/or activity of a target substance in a cell, both utilize a polypeptide of the elected Group I. "If a product claim is found allowable, process claims that depend from or otherwise require all the limitations of the patentable product may be rejoined." See M.P.E.P. § 806.05. Rejoinder of these claims is therefore courteously requested.

Rejection under 35 U.S.C. §102(b)

The rejection of claims 1, 51-57, and 64-67 under 35 U.S.C. §102(b) as allegedly anticipated by Isaac et al. (US 6,372,211) is respectfully traversed.

In levying the anticipation rejection, the Office Action at page 10 contends that "Issac et al. teach a L-lysine oxidase, comprising residues 120-135 of SEQ ID NO: 2" (i.e., a protein comprising any fragment of SEQ ID NO: 2). The rejection is moot in view of Applicants' amendment of the claims. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §112, ¶1

The rejection of claims 1, 51-57, and 64-67 under 35 U.S.C. §112, first paragraph, due to allegedly lacking a written description and for failing to provide enablement is respectfully traversed.

At the outset, it is courteously submitted that the §112, ¶1 rejection of claims directed to fragments of the instant claimed polypeptides is moot in view of the amendments. Applicants' amendment of the claims is not to be construed as acquiesce to this or any other ground of rejection.

With respect to 90% identity as recited in the claims, Applicants submit that as is understood in the art, such a claim term includes a genus of biomolecules (for example, polypeptides) which share a high degree of homology and comprise similar functionality. This structural limitation is accepted in science as a basis of an identitical functionality. On this principle, numerous screening published in the art are based, in which DNA primers are generated using homologies, in order to subsequently isolate comparable,

homologous proteins from DNA libraries of various species or of various organs of the same species. Additionally, comparative studies of the homology of proteins having the same functions over different species have shown that an identity of 90%, as recited in the claims, is not even necessary. In most cases, the functionality of proteins can be established by merely comparing regions that are homologous. As such, the PTO's contention with respect to lack of written description/enablement of polypeptides that are 90% identical to a given sequence, for example, SEQ ID NO: 2 is without scientific basis.

The following arguments are provided to refute the PTO's contention that the polypeptide structures recited in Applicants' claims are large, and thus fail to comply with the written description/enablement requirements under §112, ¶1.

Written Description

Applicants courteously submit that the claims in the current form fully conform to the Written Description Guidelines issued by the USPTO. See, *Synopsis of Written Description Guidelines*, Example 9; *Enzo Biochem. Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). For example, a review of the full content of the specification indicates that an aspect of the claimed invention is the isolated nucleic acid that hybridizes to a complement of SEQ ID NO: 1, 3, or 5 under highly stringent hybridization conditions and encodes a protein with a function. The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.

Applicants' claims recite a genus of nucleic acids all of which stringently hybridize with the complement of SEQ ID NO: 1, 3, or 5. See, for example, page 12, lines 17–19. The highly stringent hybridization conditions set forth in the claim yield structurally similar polynucleotides. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention. Therefore, Applicants' claims, in view of the detailed disclosure contained in the specification, are in full conformance with the written description guidelines.

The central issue is whether specific polynucleotides that hybridize to the complement of a given polynucleotide under stringent hybridization conditions are

"reasonably obtainable" and whether one of ordinary skill in the art can determine the structure of polypeptides encoded by such polynucleotides. The instant specification provides expressed written guidance on structure(s) of such polynucleotide compounds (for example, polynucleotide sequences that are complementary to SEQ ID NOs: 1, 3, or 4). Conditions (for example, buffer compositions, temperature, and other reagents) which facilitate hybridization are also described. A skilled artisan could routinely utilize translation techniques for identifying polypeptides which are encoded by such polynucleotides (for example, using translation tools) and whether such polypeptides are commensurate with the claimed subject matter (i.e., comply with the structural aspect recited in the claims). The entire process would constitute nothing more than routineness. Applicants therefore courteously submit that the instant claims satisfy the criteria under *Enzo* and thus satisfy the statutory requirements under §112, ¶1.

It is therefore courteously submitted that Applicants' claims in the current form, with adequate support from the specification, fully comply with the written description guidelines, as specified by the USPTO. Withdrawal of the rejection is respectfully requested.

Enablement

With respect to the enablement rejection, Applicants invite the Examiner to review a recent precedential opinion issued by the United States Board of Patent Appeals and Interferences (*Ex parte* Kubin), a copy of which is enclosed herewith.

The facts in Kubin are applicable to the present case. In *Kubin*, the Examiner contended that "at least 80% identity language" in the absence of any working examples, other than a few representative species, fails to provide enablement of the claimed genus of molecules. See, page 10 of *Ex parte* Kubin. The Examiner alleged that specification did not teach "which 20% . . . of amino acid residues should be changed in order to maintain the biological functions." In response, Appellants argued that the specification disclosed "in detail how to:

(1) make variants of SEQ ID NOs: 1 and 2;

(2) calculate the percent identity between SEQ ID NOs: 1 and 2 and the variant sequence; and

(3) test the variant sequence to determine [functional activity]."

See, items 23 and 24 at page 13. Appellants further argued that in view of the high level of skill in molecular biology, methods of making the claimed nucleic acid sequences and screening for activity [were] known in the art and described in the specification and that the "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art." The amount of experimentation involved would have been routine and not undue. See, items 27–30 at page 14.

The Board of Patent Appeals and Interferences in reversing the enablement rejection concluded:

> "The amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art. *See, e.g., Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1360, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998) ("test [for undue experimentation] is not merely quantitative . . . if it is merely routine"). A "patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). Thus, we conclude the Specification would have enabled the full scope of claim 73. (Emphasis added)

Likewise in the present application, Applicants disclose a genus of oxidase polypeptides having at least 90% identity to one or more polypeptide sequences, whose primary structure is disclosed (i.e., polypeptide of SEQ ID NO: 2, 4 or 6 and/or polypeptides that are encoded by the polynucleotide sequence set forth in SEQ ID NO: 1, 3, or 5). The specification provides detailed guidance with respect to methods of obtaining other polypeptide sequences which are commensurate with the claims. In particular, methods of hybridization can be used to isolate sequences which hybridize under stringency conditions set forth in the specification. Conditions (for example, buffer compositions, temperature, and other reagents) which facilitate hybridization are also described. A skilled artisan could routinely utilize translation techniques for identifying polypeptides which are encoded by such hybridizing polynucleotides (for example, using translation tools) and whether such polypeptides would meet the structural limitations recited in Applicants' claims (for example, having at least 90% sequence identity along the entire length to the polypeptide of SEQ ID NO: 2, 4, 6). Polypeptide sequences which meet this aspect could then be expressed and assayed

for claimed oxidase activity using techniques which are described in Applicants' own specification. See, for example, the disclosure contained in Example 7 at page 46 of the originally-filed specification. It would be routine that such polypeptides could be isolated and used by one of ordinary skill in the art using the methods recited in the instant application. Therefore, the level of "experimentation involved to produce other sequences within the scope of the claims" and thus to practice the full scope of the claims would have been "well within the skill of those in the art."

In view of the above remarks, it is respectfully submitted that Applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with an effort that is routine within the art. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

Therefore, all the rejections under §112 must be withdrawn.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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Encl:

1. *Ex parte* Kubin (B.P.A.I. 2007)